

## **REMARKS**

The Declaration has been objected to for its failure to clearly recite the citizenship of one of the inventors, Patrick Roussel.

A supplemental Declaration, attached herewith, executed by Mr. Roussel on April 10, 2007, sets forth his address and citizenship of Mr. Roussel.

The outstanding Official Action objects to the claim of priority from earlier filed related applications. To overcome this objection, applicants have amended the specification to indicate that the present application is a U.S. national phase, filed under 35 U.S.C. §371, of International application, Serial No. PCT/EP2003/05094, filed December 4, 2003, which claims benefit of U.S. provisional patent application, Serial No. 60/434,952, filed December 19, 2002.

In addition to the aforementioned amendment to the specification, wherein the priority related applications are set forth, the specification has been further amended to include an abstract. The inclusion herewith of an abstract, as required by 37 C.F.R. §1.72(b), overcomes the objection to the specification predicated on the absence of that required portion.

Of the seventeen claims, Claims 34-50, submitted for examination in this application, five of them, Claims 44-48, have been indicated to be allowable. These claims remain in the application. The remaining claims, Claims 34-43, 49 and 50, stand rejected on formal grounds. Applicants have amended the rejected claims and submit that all of these rejected claims, as amended, are patentable over the formal grounds of rejection imposed in the outstanding Official Action.

Two formal grounds of rejections are imposed in the outstanding Official Action. The first of these is directed to Claims 34-43, 49 and 50. Claims 34-43, 49 and 50 stand rejected, under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

Specifically, the test set forth in In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988) is deemed unmet by the disclosure provided in the specification of the present application. The Official Action points out that the specification demonstrates activity, as manifested by protein kinase inhibition, specifically Cdk2/Cyclin A inhibition activity, for only two compounds, N[5-(2,2-dimethylpropanoyl)-6,6-dimethyl-1,4,5,6-tetrahydropyrrolo[3,4-c]pyrazol-3-yl]-4-fluorobenzamide and N-[5-(2,2-demethylpropanoyl)-1,4,5,6-tetrahydropyrrolo[3,4-c]pyrazol-6-spirocyclopropan-3-yl]-4-fluorobenzamide.

The Official Action argues that these two compounds, as well as the reference compound, are within the scope of generic formula (I) when R<sub>1</sub> is alkyl. As such, the Official Action avers that there is no teaching or guidance present in the specification or prior art that suggest that replacement of an alkyl group as R<sub>1</sub> with a 5 to 7 membered heterocyclic ring would provide inhibitory activity for Cdk2/Cyclin A *in vitro*.

This formal ground of rejection is supplemental with other criticisms lodged in regard to the scarcity of biological data supporting the efficacy of the class of compounds encompassed by generic formula (Ia) in treating cell proliferative diseases.

Applicants have considered this ground of rejection and enclose herewith a Declaration under 37 C.F.R. §1.132, executed by Marina Ciomei, an applicant of this application, demonstrating efficacy, as manifested by the low concentrations of a multiplicity of compounds within the scope of formula (Ia) or (Ib) in providing an IC<sub>50</sub> Cdk2/Cyclin A inhibitory effect.

Applicants submit that this Declaration overcomes the rejection predicated upon the alleged failure of the present specification to meet the enablement requirement. Clearly, the

large number of compounds meeting the IC<sub>50</sub> test at low concentration evidence the inhibitory effect *in vitro* of these compounds.

The second formal ground of rejection is directed to Claims 49 and 50. Claims 49 and 50 stand rejected, under 35 U.S.C. §112, second paragraph, as being indefinite.

The basis for indefiniteness of Claim 49 and 50 is the absence of the specific chemotherapeutic agents recited in those claims. That is, the recitation of a chemotherapeutic agent is indefinite in the absence of a specific recitation of specific chemotherapeutic compounds.

Applicants have amended Claims 49 and 50 to include a Markush group of chemotherapeutic agents within the contemplation of the pharmaceutical composition of Claim 49 and the chemotherapeutic agents utilized in the product or kit of Claim 50. Support for the recitation of the recited chemotherapeutic agents is provided in the originally filed specification at Page 36, line 23 to Page 37, line 7.

The above remarks establish that the two grounds of rejection imposed in the outstanding Official Action, the two aforementioned formal grounds of rejection, have been overcome. Reconsideration and rescinding of these grounds of rejections is therefore deemed appropriate. Such action is respectfully urged.

The above amendments and remarks, when taken with the enclosed Declaration under 37 C.F.R. §1.132, establish the patentable nature of all the claims currently in this application. Notice of Allowance and passage to issue of these claims, Claims 34-50, is therefore respectfully solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Peter I. Bernstein', with a stylized, flowing script.

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Enclosure: Supplemental Declaration and Declaration under 37 C.F.R. §1.132